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High-density electroencephalographic recordings during sleep in children with disorders of consciousness

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ABSTRACT

Introduction: A large number of studies have investigated neural correlates of consciousness in adults. However, knowledge about brain function in children with disorders of consciousness (DOC) is very limited. We suggest that EEG recordings during sleep are a promising approach. In healthy adults as well as in children, it has been shown that the activity of sleep slow waves (EEG spectral power 1–4.5 Hz), the primary characteristic of deep sleep, is dependent on use during previous wakefulness. Thus the regulation of slow wave activity (SWA) provides indirect insights into brain function during wakefulness.
Methods: In the present study, we investigated high-density EEG recordings during sleep in ten healthy children and in ten children with acquired brain injury, including five children with DOC and five children with acquired brain injury without DOC. We used the build-up of SWA to quantify SWA regulation.
Results: Children with DOC showed a global reduction in the SWA build-up when compared to both, healthy children and children with acquired brain injury without DOC. This reduction was most pronounced over parietal brain areas. Comparisons within the group of children with DOC revealed that the parietal SWA build-up was the lowest in patients showing poor outcome. Longitudinal measurements during the recovery period showed an increase in parietal SWA build-up from the first to the second sleep recording.
Conclusions: Our results suggest that the reduced parietal SWA regulation may represent a characteristic topographical marker for brain network dysfunction in children with DOC. In the future, the regulation of SWA might be used as a complementary assessment in adult and paediatric patients with DOC.
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1. Introduction

After severe traumatic or non-traumatic brain injury surviving patients often show disorders of consciousness (DOC). Traditionally, DOC are categorized into coma, in which patients are completely unarousable and unresponsive, vegetative state (VS) defined by the re-emergence of spontaneous eye-openings and minimally conscious state (MCS), in which patients start to show non-reflexive responses to stimuli. In clinical practice, the gold standard for the diagnosis of DOC is the use of behavioural assessment scales like the Coma Recovery Scale — Revised (Giacino et al., 2004). Such assessments are very challenging as a lack of motor functions, receptive aphasia or fluctuations in arousal might lead to false negative results and consequently to a misdiagnosis (Giacino et al., 2009). Hence, much effort has focused on the development of complementary methods to detect neural correlates of consciousness. Functional neuroimaging and electrophysiological measurements in patients with DOC and healthy subjects have provided novel insights into neurobiological aspects of consciousness (for a review see Giacino et al., 2014). While functional MRI and PET may not always be available in the clinical setting, EEG measurements can easily be performed at the bedside. Another advantage of EEG is the possibility of long-duration measurements including sleep. Such long-duration measurements are especially convenient, when assessing patients with DOC, as these patients typically show frequent fluctuations in the level of arousal (Forgacs et al., 2014).

In patients with DOC the presence or absence of normal sleep features such as different sleep stages, sleep spindles and sleep slow waves has been associated with behavioural outcome and was hypothesized to reflect global functional brain integrity (Avantaggiato et al.,

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2015; Cheliout-Heraut et al., 2001; Cologan et al., 2013; de Biase et al., 2014; Landsness et al., 2011; Malinowska et al., 2013; Rossi Sebastiano et al., 2015). More specifically, sleep spindles and sleep slow waves are known to involve thalamocortical and corticocortical circuits (e.g., Riedner et al., 2011; Schabus et al., 2007) and thus, might be suitable markers for preserved thalamocortical and frontoparietal connectivity, which in turn has been related to consciousness (Laureys and Schiff, 2012).

While, in recent years, many complementary neurophysiological methods for the assessment of DOC have been investigated in adults, very few have been applied to children. In fact, the only studies reporting more than single cases, investigated the presence or absence of sleep stages and sleep spindles in children with DOC (Avantaggiato et al., 2015; Cheliout-Heraut et al., 2001). Compared to adult patients, paediatric patients hold the additional difficulty that differences in brain activity result not only from brain injury but also depend on brain maturation. During development, the brain undergoes critical anatomical and functional maturation processes, such as synaptic pruning and changes in functional network efficiency (e.g., de Bie et al., 2012; Huttenlocher and Dabholkar, 1997). Therefore, if applied in children, neurophysiological correlates of consciousness have to account for maturational differences.

EEG recordings during sleep might be a promising approach to investigate patients with DOC. It has been shown that the activity of sleep slow waves (EEG spectral power 1–4.5 Hz), the primary characteristic of deep sleep (Borbely and Achermann, 1999), is dependent on use during previous wakefulness. This use-dependent regulation of slow wave activity (SWA) is best seen on a local level. Studies investigating SWA across the scalp found local increases over brain areas that had been used extensively (Kattler et al., 1994) or were involved in a learning task, prior to sleep (Huber et al., 2004; Wilhelm et al., 2014). Accordingly, when the use of specific brain areas was prevented (i.e., arm immobilization) SWA was locally decreased (Huber et al., 2006).Thus, the local regulation of SWA might serve as an indirect measure of the activity level of specific brain areas during wakefulness. Interestingly, the scalp distribution of SWA also shows regional differences in the course of development (Kurth et al., 2010). From early childhood to late adolescence the location of maximal SWA undergoes a shift from posterior towards anterior brain regions. These changes were proposed to reflect cortical brain maturation.

In our study, we recorded sleep in ten children with acquired brain injury (five with DOC, five without DOC) using high-density EEG. We investigated the regulation of SWA across the scalp and compared children with DOC to both, healthy children and children with acquired brain injury without DOC. For such comparisons high-density EEG is especially convenient, as the high spatial resolution allows us to detect local alterations in brain activity (Lustenberger and Huber, 2012). We hypothesized that local differences in sleep SWA regulation might represent markers for brain network dysfunction in children with DOC. Longitudinal measurements in children with DOC could further support our hypothesis and might even provide prognostic information.

2. Materials and methods

2.1. Patients

Ten children with acquired brain injury due to traumatic brain injury or stroke participated in the study, including five children with DOC (mean age 10 years, SD 4.3 years, range 4–14 years of age, two girls and three boys) and five age- and gender-matched children with acquired brain injury without DOC (mean age 10 years, SD 4.3 years, range 4–14 years of age, two girls and three boys). Demographic and clinical characteristics of the patients with DOC are shown in Table 1. Patients without DOC are described in Supplementary Table 1. Medication is documented in Supplementary Tables 2 and 3. All patients were recruited from the Rehabilitation Centre for children and adolescents in Affoltern am Albis in Switzerland over a period of three years. The participation rate was high. During the recruitment period, six patients with DOC were admitted to the rehabilitation centre. Five of them participated in the study. Parents from all patients gave written informed consent. Patients with acquired brain injury without DOC gave verbal consent. The study was approved by the local ethics committee.

2.2. Healthy subjects

We selected ten age- and gender-matched healthy children (mean age 10 years, SD 4.1 years, range 4–14 years of age, four girls and six boys) from earlier studies (Kurth et al., 2010; Pugin et al., 2015).

2.3. Behavioural assessment

Patients with DOC were assessed by a trained neuropsychologist (ALM with clinical training at the Coma Science Group in Liège, Belgium) using the Coma Recovery Scale-Revised (Giacino et al., 2004). This scale provides scoring rules for observable behaviour during auditory, visual, motor, oromotor, communication and arousal testing and categorizes patients into VS, MCS and emergence from MCS. During the week of the sleep recording, the Coma Recovery Scale-Revised was performed daily. The diagnosis was based on the best result (Table 1).

Table 1
Demographic and clinical characteristics of patients with DOC.

Patient: age, gender	Aetiology·pathology	S1 time since insult	S1 CRS-R diagnosis (total score)	Time interval S1–S2	S2 CRS-R diagnosis (total score)
DOC 1: 4 y, F	Shiga-like toxin-producing *E. coli* haemolytic-uremic syndrome, stroke (bilateral anterior and middle cerebral artery including basal ganglia)	5 months	MCS (9)	16.1 months (S2 not analysed due to epileptic activity)	MCS (9)
DOC 2: 7 y, F	Tumour resection (hypothalamic pilocytic astrocytoma), stroke (right basal ganglia, right internal capsule, left pons)	1.1 years	MCS (16)	Deceased	Deceased
DOC 3: 12 y, M	Diabetic ketoacidosis, generalized cerebral oedema, brain herniation, stroke (bilateral basal ganglia, bilateral internal capsule, bilateral cerebral crus, bilateral thalamus)	4 months	Emergence from MCS (22)	1.5 months	Fully conscious
DOC 4: 13 y, M	Traumatic brain injury, right frontoparietal and frontotemporal subdural haematoma, contusion (right cerebellum), cerebral oedema (midbrain, basal ganglia), haemorrhage (corpus callosum, brain stem), shearing injuries (subcortical, basal ganglia)	4 months	MCS (11)	4 months	Emergence from MCS (18)
DOC 5: 14 y, M	Traumatic brain injury, multiple shearing injuries (right corpus callosum, right basal ganglia, right thalamus, right midbrain), bilateral frontopolar and right frontobasal contusions	3 months	MCS (13)	4.9 months	Fully conscious

S1 = sleep recording first night; S2 = sleep recording second night; CRS-R = Coma Recovery Scale Revised; F = female; and M = male.

2.4. High-density electroencephalographic sleep recordings

Night sleep was recorded at the bedside in ten patients who had been admitted to the rehabilitation centre after acquired brain injury. In four out of the five patients with DOC, a second sleep recording was performed at a later time point (see Table 1). We used a high-density EEG system (Electrical Geodesics Inc., 128 electrodes) including two external electrodes for the submental EMG. Recordings were sampled at 500 Hz and referenced to the vertex (Cz). Offline the EEG data was band-pass filtered between 0.5 and 40 Hz and the EMG data between 20 and 40 Hz. All data were down-sampled to 128 Hz. EEG spectral power was calculated for 20 s epochs (fast Fourier transform routine, Hanning window, average over five consecutive 4 s epochs). Epochs containing artefacts were semi-automatically and visually rejected (Huber et al., 2000). Electrodes showing poor EEG signal quality were excluded. Data from all good quality electrodes above the ears were average-referenced (Kurth et al., 2010).

2.5. Analysis of sleep recordings

Sleep stages for 20 s epochs were visually determined based on standard criteria provided by the American Academy of Sleep Medicine (Iber et al., 2007). Fig. 1 and Supplementary Fig. 1 show individual sleep scorings and SWA (EEG spectral power 1–4.5 Hz) over a central derivation across the night. In healthy subjects, SWA is highest at the beginning of the night and declines towards the end of the night (Supplementary Fig. 1). This decline of SWA is supposed to reflect the dissipation of sleep pressure (Borbely and Achermann, 1999). Another sensitive measure for sleep pressure is the build-up of SWA. Within single non-REM sleep episodes, SWA shows an initial build-up and a subsequent decline. Similar to SWA itself, the rise rate of the SWA build-up decreases across non-REM sleep episodes (Supplementary Fig. 1). Accordingly, the build-up is steeper in episodes at the beginning of the night when sleep pressure is highest (Borbely and Achermann, 1999). SWA and the build-up of SWA are both known to be regulated in a use-dependent manner. After prolonged wakefulness the amount of SWA is increased and the build-up of SWA within non-REM sleep episodes is faster (Borbely and Achermann, 1999). For our analysis, we used the build-up of SWA as a measure for the use-dependent SWA regulation. In healthy adults and children, the build-up of SWA is commonly calculated by estimating the slope of the SWA time course during the first non-REM sleep episode, including approximately 30 min of non-REM sleep, using a linear fitting approach (e.g., Bachmann et al., 2012; Tarokh et al., 2012). As patients with DOC typically show fragmented sleep conditions, we developed the following approach to quantify SWA regulation during multiple shortened periods of SWA: After artefact removal, we calculated the mean SWA for 1-min epochs across the entire night, including all sleep stages. Next, we quantified the SWA build-up for 9 min episodes. To do so we estimated the slope of a linear fit (MATLAB function *polyfit*, MathWorks) including 9 consecutive 1-min epochs of SWA. Then we selected the four episodes of maximal SWA build-up, i.e. maximal slope (Fig. 2 and Supplementary Fig. 2). The threshold of 9 min was based on the maximal SWA build-up duration reached in the patient showing the highest sleep fragmentation (Figs.1 and 2: DOC 4). We used four episodes to increase the amount of data included in the analysis. In one patient (DOC 3) we only determined three episodes of SWA build-up due to a shortened total sleep time (<3 h). We averaged the SWA build-up across all episodes within individuals. Missing values from electrodes excluded because of poor data quality were interpolated. We mapped the SWA build-up including all electrodes above the ears (109 electrodes) for all patients and healthy subjects (patients with DOC and the five closest age-matched healthy subjects shown in Fig. 3). We used relative values to investigate topographical aspects irrespective of absolute SWA build-up differences. These relative SWA build-up values were obtained by calculating the ratio between the SWA build-up from each electrode within the topography and the average across the topography. In order to investigate differences within the group of patients with DOC, we calculated age-normalized relative SWA build-up values. For this purpose, we calculated the ratio of the relative SWA build-up between individual patients with DOC and the mean over their respective matched healthy subjects (Fig. 5).

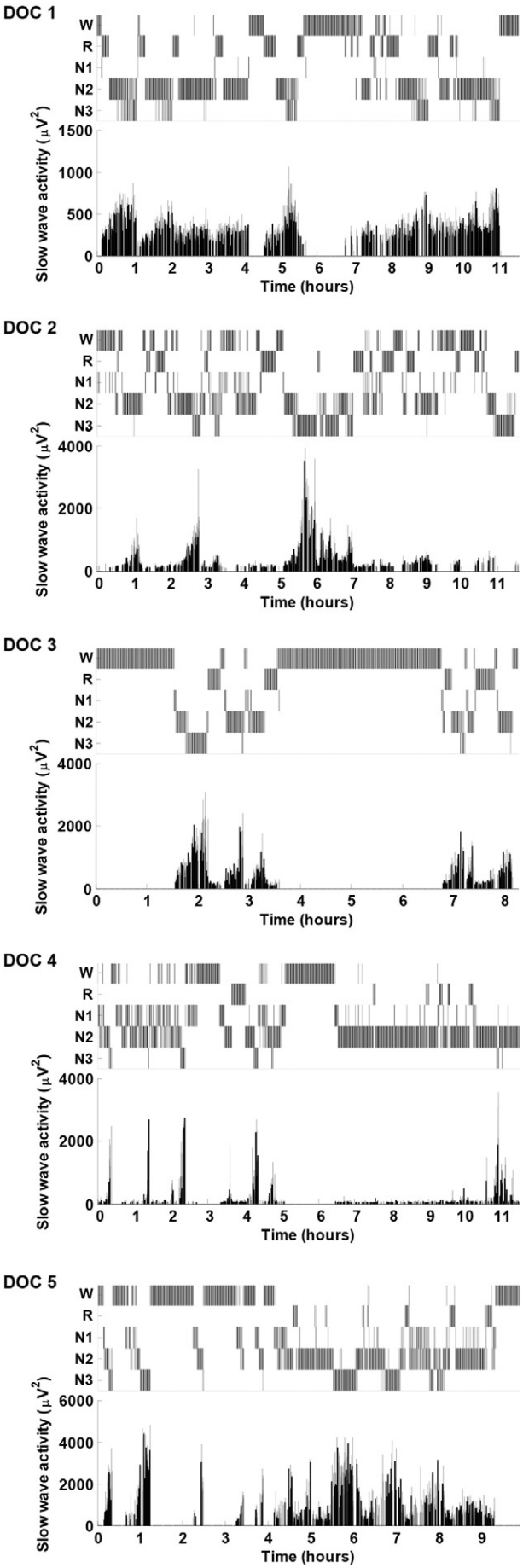
For our analysis, we decided to use the build-up of SWA rather than SWA itself. This decision was based on the assumption that in patients with acquired brain injury SWA might be confounded by the presence of lesion-related slow-oscillations (also described as pathological slowing of the EEG) arising as a result of cortical deafferentation (Lemieux et al., 2014; Steriade et al., 1993). First, we assume that pathological low frequency activity is continuous and second, we do not expect this activity to show changes related to previous wakefulness. In contrast, sleep SWA is modulated across the night as a function of previous wakefulness. Within single non-REM sleep episodes, SWA shows a build-up and a subsequent decline (Borbely and Achermann, 1999). Moreover, the build-up of SWA is known to show changes related to brain activity during previous wakefulness (Borbely and Achermann, 1999). We used the build-up of SWA instead of SWA to minimize the confounding effect of pathological low frequency activity. To verify the accuracy of our approach we investigated the topographical contrast between relative SWA across the night and relative SWA build-up in all patients and healthy subjects. We calculated the ratio between relative SWA and SWA build-up and determined individual clusters of four electrodes showing maximal values (i.e., higher relative SWA than SWA build-up). We then mapped the topographical cluster distribution for patients and healthy subjects (Supplementary Fig. 3). The clusters from healthy subjects were all located over frontocentral brain areas. Conversely, the clusters from patients with acquired brain injury were widely scattered over the scalp. Thus, the relationship between SWA and SWA regulation indeed was changed in patients. This finding supports our assumption of confounded SWA after brain injury and confirms our choice to use the build-up of SWA for our analysis.

2.6. Statistics

Topographical group comparisons of the SWA build-up between patients with DOC and patients with acquired brain injury without DOC were performed using an unpaired two-tailed *t*-test for each electrode ($P < 0.05$). Group comparisons between patients with DOC and healthy subjects were performed using a combinatorial approach. We had two age- and gender-matched healthy subjects for each patient with DOC. This resulted in 32 possible group combinations for the healthy control group. We performed 32 two-tailed unpaired *t*-tests for each electrode. Topographical differences were reported significant when the 95% confidence interval of the *p*-value was below 0.05.

3. Results

At the time of the first sleep recording, four patients were in an MCS, one patient had emerged from MCS two days prior to the sleep recording (Table 1). We found different sleep stages to be present in all of them (Fig. 1). However, when compared to healthy subjects we found major differences in terms of sleep fragmentation and duration of waking after sleep onset (see also Supplementary Fig. 1). We developed an adapted calculation for the build-up of SWA to quantify SWA regulation (see Section 2 for details). In healthy children, we found expected age-specific topographical distributions with a maximal SWA build-up over more posterior brain areas in younger children and more anterior brain areas in older children respectively (Fig. 3, lower row; see Kurth et al., 2010 for a detailed description of typically developing children and adolescents). In a first step we assessed group differences on a global level. Children with DOC showed severely altered patterns (Fig. 3, upper row) and lowest SWA build-up values (Fig. 4, upper row). Both group comparisons (i.e., patients with DOC vs. patients with acquired



brain injury without DOC and patients with DOC vs. healthy subjects) showed significant differences over large areas of the brain. In a next step we investigated local differences between the groups using normalized values of SWA. The relative SWA build-up in patients with DOC was significantly lower over parietal brain areas (Fig. 4, lower row) when compared to the two other groups. Additionally, we found a small frontal cluster in healthy subjects and a single frontal electrode in patients with acquired brain injury without DOC showing significantly higher values than in patients with DOC. In a final step, using age-normalized relative SWA build-up values, we investigated differences in the parietal electrode cluster between individual patients with DOC. We found the lowest values in patients showing poor outcome (Fig. 5, Table 1). In the three patients showing recovery, we found an increase in age-normalized relative SWA build-up values from the first to the second sleep recording. The second sleep recording from patient DOC 1 had to be excluded from the analysis, due to continuous epileptic activity.

4. Discussion

In the present study, we investigated topographical patterns of SWA regulation in children with DOC. We found a widespread reduction of SWA build-up when compared to both, healthy subjects and patients with acquired brain injury without DOC. These findings indicate a global dampening of regulatory aspects of sleep in patients with DOC. The topographical distributions of relative SWA build-up revealed local differences. Patients with DOC showed a reduced relative SWA build-up over parietal brain areas and over a smaller frontal brain area when compared to the two other groups. As no patient had a local damage in parietal brain areas, we suggest that the parietal reduction in the SWA build-up does not simply reflect brain damage but rather represents a topographical marker for network dysfunction in patients with DOC. Moreover, the topographical distribution of the SWA build-up differed between patients with DOC and patients without DOC. This finding indicates that the presence of DOC and the parietal reduction in SWA build-up are likely not determined by specific lesions but rather by whether or not network function is preserved. Our results are in agreement with a recent high-density EEG study that found resting state spectral power measures over frontal and parietal brain regions to be sensitive indices of consciousness in adults (Sitt et al., 2014). Also functional MRI and PET studies identified frontoparietal networks as being critically involved in DOC (for a review see Laureys and Schiff, 2012). Thus, in patients with DOC, network dysfunction indeed seems to involve similar brain areas during wakefulness and sleep.

Considering the current state of research in the field, Laureys and Schiff (2012) proposed a model of consciousness accounting for transitions across the continuum of DOC. They suggest frontoparietal and thalamocortical networks to be modulated by a mesocircuit including the frontal cortex, the thalamus and the basal ganglia. Interestingly, frontoparietal and thalamocortical networks are also known to be involved in the generation and propagation of sleep slow waves (Massimini et al., 2004; Murphy et al., 2009). These findings support the hypothesis that network dysfunction related to DOC during wakefulness is associated with a similar pattern of alterations in SWA regulation during sleep.

In our paediatric patient population, the reduced relative SWA build-up over parietal brain areas was a consistent finding across a wide age range (4 to 14 years of age). Thus, we suggest that functional networks underlying consciousness might be similar throughout childhood and adulthood. Indeed, functional networks were found to be already

Fig. 1. Hypnogram and slow wave activity (SWA) time course across the night for five patients with DOC. The sleep scoring includes wake (W), rapid eye movement sleep (R), NREM sleep stages N1, N2 and N3. SWA is shown for a central derivation. See Supplementary Fig. 1 for the hypnogram and SWA time course for the other groups of subjects.

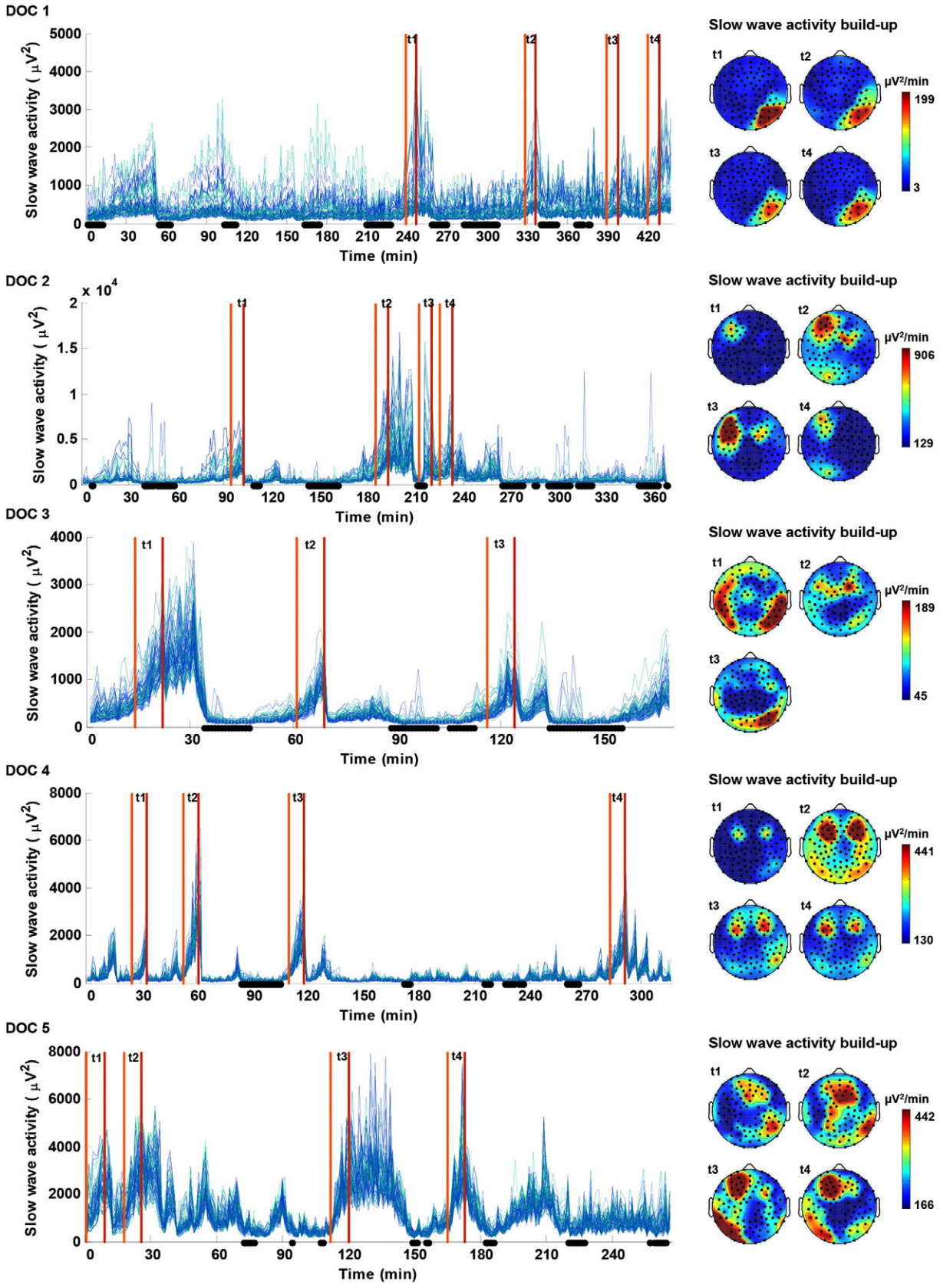


Fig. 2. SWA time course and scalp distribution of SWA build-up for five patients with DOC. SWA is shown across 1 min epochs. Each line represents the SWA time course for one electrode. Only artefact free sleep epochs were included. Black dots on the bottom line indicate epochs of REM sleep. Vertical lines in orange and magenta mark beginning and end of the four 9 min episodes of maximal SWA build-up. Topographical plots (right) show the distribution of the SWA build-up for the four determined episodes. Colour coding was individually scaled in order to optimize the visualization of topographical patterns (maximal values in red, minimal values in blue). See Supplementary Fig. 2 for same plots of the other groups of subjects.

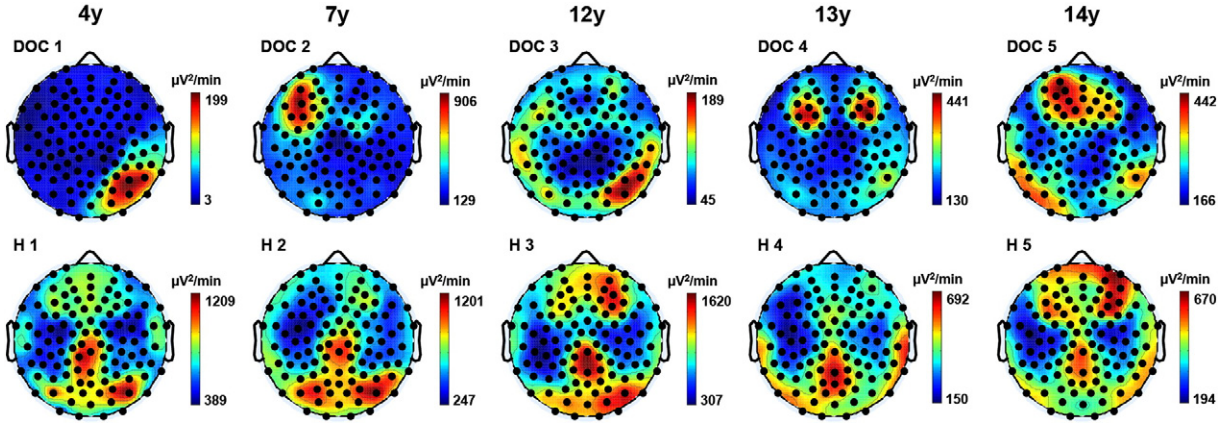


Fig. 3. Scalp distribution of SWA build-up for five patients with DOC and five age- and gender-matched healthy subjects (H). Age is indicated in years (y).

present in childhood, yet showing an immature organization (de Bie et al., 2012; Fair et al., 2007). Consequently, the proposed network model of consciousness may also be applied to children, even though network connectivity is likely to show age-dependent differences. Furthermore, the fact that all children with DOC had lesions in the area of the basal ganglia (see Table 1) indicates that the proposed mesocircuit might also play a critical role in paediatric patients with DOC.

In our study, we focussed on regulatory aspects of brain activity during sleep. A previous study in adult patients with DOC used the decline of SWA across the night as a maker for sleep regulation (Landsness et al., 2011). However, we did not see this typical trajectory of SWA in our young patients (see Fig. 1). Possible reasons would be daytime sleep or night sleep fragmentation. For our analysis, we used the build-up of SWA to quantify use-dependent SWA regulation. We developed an adapted calculation to account for sleep fragmentation including four episodes of 9 min SWA build-up (see Section 2 for details). This episode duration was an optimal trade-off between using episodes of maximal possible duration and including multiple episodes to obtain a total duration of approximately 30 min (i.e., the same amount of data commonly used in healthy subjects). However, in other populations, the optimal trade-off might be different (e.g., three episodes of 12 min SWA build-up). Nevertheless, the basic principle to determine this optimum should stay the same. In our population, we further tested whether the different episodes included in the analysis were comparable. We randomly selected one out of the four 9 min episodes in each patient and healthy subject and calculated group differences. Repeating this procedure we consistently obtained significant group differences over parietal brain areas (data not shown). Thus, averaging the SWA build-up across episodes seems to be appropriate.

The local regulation of SWA has been related to learning tasks prior to sleep (Huber et al., 2004; Wilhelm et al., 2014). The fact that learning is known to induce plastic changes (for a review see Dayan and Cohen, 2011) supports a current hypothesis that SWA regulation might not just reflect brain use but more specifically, brain plasticity (Tononi and Cirelli, 2014). Neuronal plasticity is also known to play a critical role in brain reorganization processes after acquired injury (Wieloch and Nikolich, 2006). In this latter context, SWA regulation in patients with acquired brain injury might indicate local capacities for functional or even structural brain reorganization. The finding that in patients with DOC a higher parietal SWA build-up was associated with a better outcome would support this assumption since a higher plastic capacity should favour recovery.

A limitation of our study is the small sample size. However, our findings were consistent across patients with different aetiologies and across a wide age range (4–14 years) suggesting a robust pattern. Another limitation is that medication is a possible confounding factor. Only patients with DOC were treated with benzodiazepines. Since benzodiazepines are known to decrease SWA (Arbon et al., 2015; Borbély et al., 1985; Dijk et al., 1989), the patient's global reduction in absolute SWA build-up might, at least partially, be due to medication. However, differences in the relative distribution of the SWA build-up should be less influenced by benzodiazepines as it can be assumed that benzodiazepines have a rather global effect across the entire brain.

Further studies investigating brain activity in children with DOC are needed to improve our understanding of the pathophysiological

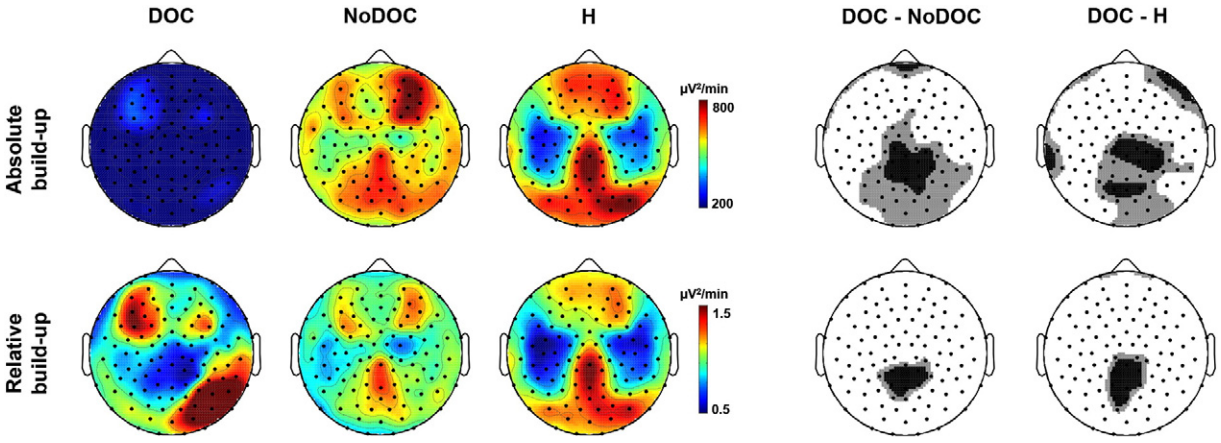


Fig. 4. Left: Scalp distribution of absolute (top row) and relative (bottom row) SWA build-up for patients with DOC, patients with acquired brain injury but without DOC (NoDOC) and healthy subjects (H). Values were colour coded using the same scale for all three groups. Right: Significant group differences in absolute (top row) and relative (bottom row) SWA build-up (in black $p < 0.01$, in grey $p < 0.05$).

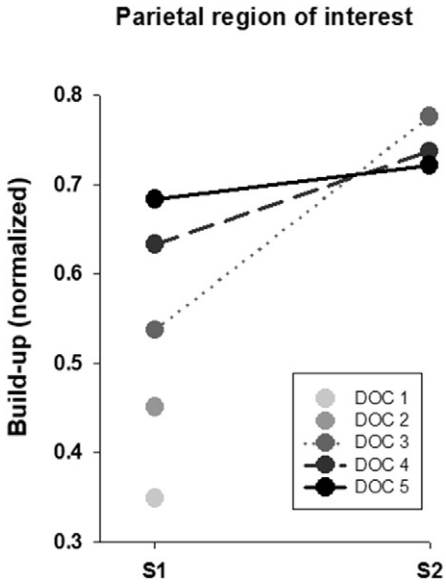


Fig. 5. Relative SWA build-up (age-normalized) in the parietal electrode cluster for patients with DOC: five patients at the time of the first sleep recording (S1) and three patients at the time of the second sleep recording (S2). Age-normalized values were obtained by calculating the ratio between individual patients and the mean over their respective matched healthy subjects.

mechanisms. Such knowledge is crucial to provide accurate diagnosis and prognosis and to guide and evaluate potential treatments. From a clinical perspective, our results suggest that high-density EEG recordings during sleep might be a suitable method to complement behavioural assessments in children with DOC. Residual parietal SWA regulation might provide additional diagnostic as well as prognostic information. On the one hand, this measure might be a marker for network function related to consciousness levels, on the other hand, it might indicate plastic capacity related to outcome. Potential therapeutic implications could imply local brain stimulation over parietal regions using, for example, transcranial direct current stimulation (tDCS) during wakefulness or transcranial oscillatory direct current stimulation (toDCS) during sleep. In adult patients with DOC, tDCS over the left dorsolateral prefrontal cortex improved behavioural performance (Thibaut et al., 2014). In children with attention-deficit hyperactivity disorder (ADHD), frontal toDCS during sleep increased the activity of sleep slow oscillations and improved memory performance (Prehn-Kristensen et al., 2014).

Although high-density EEG is currently a research method, it can easily be applied in the clinical setting. The handling of the devices is similar to standard EEG. In the future, data analysis could be standardised. Thus, if it turns out that high-density EEG recordings can provide novel, clinically relevant diagnostic and/or prognostic information, such measurements could and should be implemented in routine practice. With the traditionally available clinical measures prognostic information regarding recovery in patients with DOC, is still extremely difficult to obtain. Complementary diagnostic and prognostic information would not only be beneficial for health professionals to plan rehabilitation treatment but also meet needs of parents. The fact that despite the stressful situation, most of our patients' parents agreed to participate in the study, speaks for this assumption.

5. Conclusion

To our knowledge, this is the first study investigating topographical differences in brain activity between children with acquired brain injury and DOC, children with acquired brain injury without DOC and healthy children. We used the regulation of SWA as an indirect measure for brain activity during previous wakefulness. Our results suggest that a reduction in SWA regulation over parietal brain areas might provide a characteristic topographical marker for network dysfunction, in patients with DOC. This interpretation is in agreement with the currently proposed model of consciousness in adults. From a clinical perspective, this study is a first step towards complementary methods for diagnosis and prognosis in children with DOC. Additionally, improving our understanding of DOC could guide the development of novel therapeutic interventions. Given the small number of paediatric patients, future studies should attempt to involve multiple clinical and research centres.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.nicl.2016.03.012.

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